




The Enteric Fevers

1800-1920

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SYDNEY WATSON SMITH

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Being the Sydney Watson Smith
Lecture for the year 1954 delivered
in the Hall of the Royal College of
Physicians of Edinburgh on 10th
November by Adam Patrick, M.A.,
M.D., LL.D., F.R.C.P. (Edin. and
Lond.), F.R.F.P.S.

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Mr. President and Fellows, I thank the President and Council for having appointed me to deliver this lecture for 1954.

Sydney Watson Smith came of a well-known Dundee family, and as a boy went to the High School there. When he became a student, he took some of his classes at St. Andrews University, but his main training was in Edinburgh, where he graduated in 1903. He held house appointments in Dundee Royal Infirmary, and in 1907 he settled in practice in Dundee. While serving with the R.A.M.C. in the First World War he had an illness which caused him to be invalided out in 1918. Because of this illness he went to Bournemouth when the war was over, and after five years in general practice became a consulting physician, with an interest in dermatology as well as in general medicine. In 1925 he graduated M.D. at Edinburgh with a thesis entitled "The Factors which determine Distribution in Cutaneous Eruptions." He became a Fellow of both this and the London Royal College of Physicians, and in 1934 he was elected President of the British Medical Association, which in that year held its annual meeting in Bournemouth. The writer of one of his obituary

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notices in 1950 said that he was remembered as an outstandingly generous host on that occasion. He wrote the book which described the journey of the B.M.A. party to the 1935 annual meeting in Australia. He published also a booklet with an account of a large outbreak of milk-borne typhoid fever which occurred in Bournemouth and district in 1936. After his death in 1950, nearly the whole of his estate was bequeathed to the two Royal Colleges of Physicians, for research and other purposes.

The Nature of Typhoid

In the year 1800, which I have chosen for the commencement of this survey, there was no general recognition of more than one kind of fever. Obviously there were variations in symptoms, but it was commonly believed that these depended on the circumstances in which the fever occurred. In particular, no clear distinction had been made between typhus and typhoid, the so-called putrid malignant and the slow nervous fever; and these we know to have been the two principal endemic fevers with a high death-rate. The first half of the nineteenth century was to be filled with discussion and controversy as to whether they were one or different diseases. Yet both Murchison, the author of *A Treatise on the Continued Fevers of Great Britain*, and Hirsch, the medical historian, point out that in the eighteenth century many writers had described intestinal lesions as occurring in the slow fevers. Huxham wrote in 1739: "I cannot conclude this Essay

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on Fevers without taking Notice of the very great difference there is between the *putrid malignant* and the *slow nervous Fever*"; and again: "Could we suppose both the one and the other to arise from Contagion, which is commonly the case in pestilential and petechial Fevers, and may sometimes be so in the slow nervous?"

In the first thirty years of the nineteenth century it was the French physicians who were so active in this work of differential diagnosis. The usual pattern of their books is, first of all, an account of the signs and symptoms in a series of individual cases, and then, and this is what gave a sure foundation to their opinions, diligent examination of the organs in those patients who had died. They constantly found lesions in the lower part of the ileum, especially swelling and ulceration of the Peyer's patches, and enlargement of the glands in the mesentery. Prost in 1804 wrote of these cases under the name of "mucous fever," and in 1813 Petit and Serres published a collection of observations in forty-four cases. They referred to the ulceration of the plaques in the ileum, and the swollen mesenteric glands; and they connected this entero-mesenteric fever, as they named it, with the slow nervous fever of Huxham, and with mucous fever. The dominant figure of the time was Bretonneau, of Tours, and it is to him that the greatest part of the credit has been attributed for the recognition of specificity. He called the fever with the intestinal changes "dothienenteritis" or "dothinenteritis," "dothien" being an old Greek word for a circumscribed lesion of the skin. In 1829 he wrote

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a paper to show that it was contagious, and he mentions that from the year 1819 he had been convinced that the Peyer's structures underwent morbid change. In camp typhus, on the other hand, it had been shown that the Peyer's patches were rarely affected. In 1829 Louis published a work of nearly one thousand pages in which he described his researches into the anatomy, pathology, and therapeutics of febrile diseases over the course of the five years from 1822 to 1827. He used the word "typhoid" for the first time, and he emphasized that the lesion which is the most serious and severe, the earliest, and sometimes the only one, is always in the elliptical plaques of the small intestine. In his post-mortem reports he constantly records enlargement and ulceration of Peyer's patches, most severe at the ileo-caecal valve, and spreading upwards; enlargement of the corresponding mesenteric glands; and sometimes enlargement of the spleen. Many doctors went to Paris and studied with Louis, and they did much to spread the French views on the nature of typhoid in other countries, including Great Britain and the United States.

The action of George Eliot's novel *Middlemarch* is set about the year 1830, and several medical allusions show her acquaintance with medical affairs and problems. Mrs. Casaubon says to Dr. Lydgate: "You may still win a great fame, like the Louis and Laënnec I have heard you speak of." Earlier in the book, it is said of Lydgate: "What he really cared for was a medium for his work, a vehicle for his ideas . . . a good hospital

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where he could demonstrate the specific distinctions of fever, and test therapeutic results." It was these "specific distinctions of fever" that were a burning question among physicians.

Typhoid and Typhus

It is said by Hirsch that the appreciation of the distinction between typhoid and typhus spread slowly in Britain; and in 1849 William Jenner wrote that with few exceptions British physicians had laboured to prove that typhoid and typhus fevers were identical. Nevertheless, by that time several very good papers had been written in this country, and I should like to refer to three of them.

The first of these papers was by Robert Perry, and was published in 1836. He was a hospital physician in Glasgow, and his fever experience was large, for his conclusions were drawn from the observation of four thousand patients, and three hundred post-mortem examinations. The Glasgow Medical Society were interested in his work, and sent a committee of five of their members to see for themselves, and confirm the facts which had been put forward. Perry set out his conclusions in a list of sixteen propositions, and here are some of them:

Typhus fever is an idiopathic disease solely produced by contagion; that is, by the introduction into the system of a specific animal poison. This contagious idiopathic typhus runs a fixed course, commonly of fourteen days, which cannot be

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checked. In dothinenteritis, there is enlargement of the mucous follicles of the smaller intestine, and enlargement and ulceration of the aggregated glands of the lower third of the ileum. It may occur in combination with contagious typhus about once in every six cases, or exist as a disease by itself, and then it is characterized by the following symptoms: It commences frequently with diarrhoea. . . . The abdomen is slightly tumid. The disease may exist in every degree of mildness or severity, having no regular period of termination. It may run for two, three, or even four weeks, and terminate in a gradual restoration to health, without any sensible crisis; or the patient may sink under it with exhaustion, or by haemorrhage from the bowels; or it may end by some of the ulcers of the aggregated glands of the lower third of the ileum penetrating the coats of their intestines, and part of their contents being effused, exciting peritonitis, under which the patient sinks in the course of two, or at most, three days.

The second of the papers is by H. C. Barlow. It is entitled "On the distinction between Typhus Fever and Dothienenteritis," and was read in 1840 before the Parisian Medical Society:

Two diseases so different in their modes of origin, he says, however nearly in the course of their symptoms they may come to resemble each other, cannot be essentially identical. In dothienenteritis, diarrhoea is one of the earliest and most constant symptoms.

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It usually sets in at the beginning of the disease, and continues till its close, but it does not appear to be an essential feature. In typhus, diarrhoea is comparatively rare. In dothienenteritis there is sometimes intestinal haemorrhage. There is gurgling in the right iliac fossa, and deafness is not unusual. After eight or nine days, the typhoid eruption, consisting of lenticular rose-spots, appears on the abdomen, back, and chest. It is not an abundant rash, and is not always present. The spots come out in succession, and each lasts about four days. In typhus fever, the eruption is chiefly petechial. The duration of dothienenteritis is on an average from twenty to thirty days; in forty-three fatal cases of typhus it was twelve-and-a-half days. In typhus, the intestine and mesenteric glands show, not only a complete absence of the characteristic lesion of dothienenteritis, but an absence of any kind of lesion whatever.

After mentioning many other differences in symptoms, he concludes:

The great and crowning difference of all is the existence of a particular anatomical lesion in one, and the absence of any obvious anatomical lesion in the other. Surely two diseases which differ in all these particulars cannot be identical.

The third paper is by A. P. Stewart and is entitled "Some Considerations on the nature and pathology of Typhus and Typhoid Fever applied to the solution of

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the question of the identity of the two diseases." It appeared a few months after Barlow's, and it also had been read to the Parisian Medical Society. It is a long and admirable paper of forty-nine pages, and, judged by the number of references to it by subsequent writers, it had a great influence. He discusses the symptoms, rashes, and intestinal lesions, and is convinced, by what he has seen and read, that the diseases are distinct. Stewart, like Perry, had had his experience in the Glasgow hospitals, and had probably come under Perry's influence. A feature of Stewart's paper is his description of the rashes of typhus and typhoid:

Dr. Peebles, he says, had returned to Scotland in 1832, after a long residence in Italy, where he had been struck by the constant recurrence of an eruption in the epidemics of contagious fever. He drew the attention of the profession in Edinburgh to its presence, previously unnoticed in the typhus of that capital. It is also well known to many, he goes on, that prior to a visit which Dr. Peebles made to the Glasgow Fever Hospital in 1835, the exanthem of typhus, then found to be of general occurrence, had neither been looked for nor registered in that institution; and it was received as a new discovery. . . . The typhus rash is permanent and shows four stages, of being florid, dark, livid, and petechial. Typhoid fever also has its rash, which it is generally agreed, appears later than that of typhus. It is distinguished from the morbilliform eruption of typhus by being

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distinct, rounded, slightly elevated above the skin, and of nearly uniform size. Dr. Perry was the first whom he had heard maintain the complete difference of the two eruptions. Each typhoid spot lasts three or four days, and he had never seen a single case in which it became petechial, or even dark. On the contrary, those appearing latest were as florid as the first.

Stewart insists on the presence of the intestinal lesion in typhoid, and its absence in typhus. He quotes from one of those who believed there was only one disease, a French writer, de Claubry. De Claubry had found it difficult to explain the absence of anatomical lesions in the typhus of Glasgow and Edinburgh, but apparently he connected it with "the serious circumstances of misery and exhaustion of strength, which have so deplorably modified the constitution of the inhabitants of these wretched countries, Scotland and Ireland." Dr. A. L. Goodall, the honorary librarian of the Royal Faculty of Physicians and Surgeons, has recently published a paper on the contribution of Glasgow physicians to the differentiation of typhoid and typhus, and has been able to draw on original sources in his long and interesting account of Perry and Stewart.

The modern reader of these controversial writings is struck by the late appearance of any reference to the typhus rash, though not by the earlier failure to notice the elusive spots of typhoid. A possible reason is that the typhus petechiae were hidden among the bites of lice and fleas, which must have been very common.

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The prevalence of typhus is in itself evidence of the prevalence of the louse, and Stewart says this about it:

It is well known that for many years past, every resident clerk in the Glasgow Infirmary with very rare exceptions, many students who frequented the fever wards, several of the acting physicians, and almost all the nurses, have, at one time or other, been attacked with typhus.

The man who is best known in this country as having emphasized the difference between typhoid and typhus is William Jenner, who published a long series of articles over a course of eighteen months around the year 1850. Their full title is "Typhus Fever, Typhoid Fever, Relapsing Fever, Febricula—the diseases commonly confounded under the term Continued Fever, illustrated by cases collected at the bedside." At this time Jenner was Professor of Pathological Anatomy in University College, and assistant physician to University College Hospital. His series was of sixty-six fatal cases. When he republished his lectures and essays in 1893, he wrote in the preface:

I now publish together all the papers I have written on Fever. . . . All the facts detailed and analysed were observed and recorded at the bedside and in the dead-house by myself. While collecting some of these facts in 1847 I caught typhus fever, and three or four years later typhoid fever. I mention this because it was said at the time, "Before typhus and typhoid fevers can be said to be absolutely different diseases,

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some one must be found who has suffered from both," and I was the first, so far as I know, who at that time could be proved to have suffered from both.

A statement he quotes from Dr. Christison perhaps partially explains the long-continued difficulty in differential diagnosis. In Edinburgh, Dr. Christison had written, the intestinal lesion is seen often enough only to prevent physicians being ignorant of its characters. In Dublin it seems to be equally infrequent; while on the Continent fever without lesion of the agminated glands is so rare that many eminent practitioners have doubted the existence of such an affection. This suggests that typhus was much more prevalent in Britain, and typhoid in France.

Drains and Disease

With the identity of typhoid firmly established by the middle of the century, interest gradually turned to two other problems: how typhoid arises, and how it may be prevented. The medical writings after 1850 are now concerned not so much with symptoms and pathology as with epidemics and their possible causes. Although Bretonneau wrote in 1829 that it was a contagious disease, it was not so obviously contagious as typhus; yet evidence was accumulating that typhoid was often caused by the contamination of drinking-water by sewage. In a survey of this phase one cannot consider typhoid alone, but must look more widely at the state of the sanitation of the time. I have gone into

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this at some length to give a better idea, not only of the general state of hygiene, but also of how the people, including the doctors, viewed these matters and reacted to them.

When one reads of the numerous epidemics, the general impression is of how bad the drains were in those days. Again and again there is the story of broken drain-pipes, leaking cesspools, contaminated wells. In its article on Hygiene the 1906 edition of *Chambers's Encyclopaedia* refers to "the vile 'scamping' work in the matter of drains so prevalent in former years." I shall give two illustrative examples.

We remember that in our own time, in 1937, the burgh of Croydon had an outbreak of typhoid with nearly three hundred and fifty cases, which arose from the infection by a carrier of the water of a well under reconstruction. In 1852 Croydon had a bigger epidemic. The *Lancet* of the time gives an account of it. The Croydon local Board of Health employed a sewage engineer and the local surveyor to prepare plans to improve the sewerage and the water supply. These plans, when submitted to the General Board of Health, were, as usual, superseded by that body, who transferred to their own inspector the control of the work, by stipulating, also as usual, that no expense should be incurred without the approval of the superintending engineer. The inspector reduced the size of the local Board's planned sewers from 6 inches to 4 inches, and from 8 inches and 9 inches to 6 inches. He instituted a filter-house with perforated zinc strainers, the re-

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mainder of the sewage being discharged into the river Wandle. Three outfalls were provided, and one of these ran sewage over seventeen acres of Waterman's meadow. Fever broke out in August 1852, and continued. The *Lancet*, commenting on the report of the commissioners appointed by the Secretary of State to make an inquiry, said:

The result is conclusive in condemnation of the Board's theories. Croydon with its open drains and its thousand cesspools, unenlightened by the wisdom of Gwydyr House [the Board of Health], unvisited by the superintending inspector—old dirty ill-drained Croydon—was healthful and happy compared with the Croydon in which the presiding genius of the Board of Health has exercised its fancies, interlacing it with a network of tubular pipe drains of minimum size, and "impermeable sewers" which were constantly giving way; driving the inhabitants frantic with combined back drainage; pumping sewage into the open streets, concentrating the faecal odours of the whole town in one gigantic miasmal bouquet from a so-called filter-house, and poisoning the beautiful waters of the Wandle by discharging into it the agglomerated sullage of 10,000 inhabitants, saving only what might have been left to fester over seventeen acres of meadow within half-a-mile of the town. . . .

G. Bottomley, writing a few months earlier, had said that nothing short of main street-sewers, with the

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drains of every large house going directly into them, would be effective. He gives the number of cases in five-and-a-half months as sixteen hundred, with seventy deaths. The fever was of the gastro-enteric type.

I have quoted these descriptions to give an idea of the conservative outlook of one of the leading medical journals on important public health matters, the vigour with which they said what they thought, and the low opinion the doctors held of the endeavours of the central sanitary authorities. Indeed, in a leading article the *Lancet* said that the Board of Health might more fitly be styled the Board of Death.

The second instance I wish to mention is of a sudden outbreak of typhoid in a mansion-house in Midlothian, and is recorded by T. Sheriff. The house had been closed for some time while workmen carried out alterations for a new proprietor. The family took possession early in July 1865, and on 23rd July the first case occurred, and a number of others followed. The house, it was said, had been built about forty years earlier by one of the ablest architects of the time, and no expense was spared to render the edifice as complete as possible. There was probably no mansion-house more carefully constructed in every respect, except as to drainage. But the well which supplied all the water was situated in the kitchen court, and at a distance of less than four yards there was a cesspool into which ran three drains.

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T. J. Maclagan wrote from Dundee in 1867:

It may be generally inferred that when enteric fever becomes unusually prevalent in a locality whose water-supply and drainage are known to be good, and about which no filth is allowed to remain, the probable cause . . . is likely to be some accidental contamination of the water, or derangement of the system of drainage.

Were we to read today of such events we should be alarmed and anxious. Our ancestors of a hundred years ago were less concerned. We have seen how the doctors expressed themselves about the Croydon outbreak. The paragraph which follows shows that public opinion agreed with them. On 31st July of the present year *The Times* quoted from *The Times* of 1st August 1854, adding this explanatory note:

Parliament had rejected a bill for extending the powers of the Board of Health. *The Times* became the mouthpiece of the popular feeling against being "bullied into health." Sir Edwin Chadwick had committed the unpardonable crime of telling the truth about the sanitary condition of the great towns. Dr. Southwood Smith had supplied the unsavoury evidence.

The paragraph of 1854 reads:

The British nature abhors absolute power. . . . The Board of Health has fallen. After an irregular growth of six years, varying between too forward

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developments and sudden checks, it has finally withered like an exotic unsuited to this soil or clime. We all of us claim the privilege of changing our doctors, throwing away their medicine when we are sick of it or doing without them altogether when we feel tolerably well. The nation, which is but the aggregate of us all, is as little disposed to endure a medical tyrant. Esculapius and Chiron, in the form of Mr. Chadwick and Dr. Southwood Smith, have been deposed, and we prefer to take the chance of cholera and the rest rather than be bullied into health. Lord Seymour [who had moved the defeat of the Bill] has liberated us from this new and strange dominion. He is the William Tell who has overthrown the sanitary Gesler. . . . There is nothing a man hates so much as being cleansed against his will, or having his walls whitewashed, his pet dunghill cleared away, or his thatch forced to give way for slate, all at the command of a sort of sanitary bombailiff. It is a positive fact that many have died of a good washing, as much from the irritation of the nerves as from the exposure of the cuticle, no longer protected by dirt.

William Budd's Views

One of the most distinguished physicians in the nineteenth century was William Budd, who was born in 1811 in the village of North Tawton in Devon, where his father was in medical practice. He received his medical education in London and Edinburgh, and then in Paris, where he spent four years. He graduated M.D.

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in Edinburgh in 1838, with a gold medal thesis on acute rheumatism. Later he was physician to Bristol Royal Infirmary for fifteen years. Budd was interested in fevers, and especially in typhoid, of which he had earlier had a very severe attack. Although by this time it was evident that the occurrence of typhoid was closely connected with bad sanitation, the exact mode of its origin remained unproved, and there was a widespread belief in its spontaneous generation from dirt and filth. But many held that one case arose from another, and the principal advocate of this view was Budd. In 1856 he commented on an outbreak of fever which had occurred in the Clergy Orphan School in London, of which a "painfully interesting" account had appeared in the *Lancet* for 15th November:

There can be little doubt that the disease which is spreading is the specific fever whose simple anatomical character was first shown by Louis to be an equally specific disease of the intestinal follicles . . . a fever variously known in this country under the name of common continued, typhoid, gastric fever, and so on, but of which intestinal fever would seem to be the fitter designation. . . . This species of fever has two fundamental characteristics: (1) it is an essentially contagious disorder, and (2) by far the most virulent part of the specific poison is contained in the diarrhoeal discharges.

He had no doubt the real danger came from these excreta. "The drain," he added, "is a continuation of

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the intestine.” In another paper two weeks later he uses these words:

In saying that this fever is a contagious fever I am well aware I was making an assertion to which the great weight of medical opinion in this country is directly opposed. Not to speak of minor notabilities, the whole prestige of the Board of Health and of the London Royal College of Physicians may be cited against it.

The Pythogenic Theory

Charles Murchison, the best-known fever physician of his time, believed that typhoid might originate spontaneously from dirt. This old-fashioned view of his was rather surprising, for he was only thirty-two when his great treatise on the continued fevers of Great Britain was published. He died of aortic disease before he was fifty. In his book on fevers he cited nearly eighty names which had been given to typhoid, and invented a new one, “pythogenic fever,” meaning “generated in rottenness.” Budd would have none of it, and in three papers on the pythogenic theory in 1861 wrote:

The belief in spontaneous generation, long given up for alligators, toads, and fishes, and even in these latter days for the entozoa also, still lingers among us in its application to microscopic types. . . . Although it is becoming clear that the days of the pythogenic theory of fever are numbered, there is every reason

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to believe it will show a similar tenacity of life. Among other evidences of a still active vitality may be mentioned the attempt recently made by a distinguished physician to replace the names by which typhoid or intestinal fever has hitherto been known by the name "pythogenic" (i.e. "born of putrescence"). . . .

Budd cites instances in which pythogenic conditions existed without giving rise to disease, and goes on:

Some years ago I was taken severely to task by one of the first literary men of the day for contending that cholera is contagious. After observing that the idea had been discarded by all the great authorities, including the Royal College of Physicians and the General Board of Health, . . . he added that he wondered I was not ashamed to teach such an "immoral" doctrine. . . . In a leader which appeared in the *Medical Times and Gazette* for 9th February 1861 under the heading "Abandonment of the doctrine of the specificity of contagious diseases," the writer states that one by one authors and observers are declaring their belief that "these diseases may originate *de novo* out of the dirt and neglect which surround us." Under the inspiration of the same sentiment Miss Nightingale has added one more to the list of alleged discoveries enumerated by the editor of the *Medical Times and Gazette*. In one of the notes appended to her little book on *Nursing*, this truly eminent lady asserts that "she has seen with her

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eyes and smelt with her nose” the smallpox in the very act of formation in close rooms and overcrowded wards, where, she continued, it could not by any possibility have been “caught,” but must have begun.

This footnote of Florence Nightingale’s ends with these words:

I have seen diseases begin, grow up, and pass into one another. . . . I have seen, for instance, with a little overcrowding, continued fever grow up; and with a little more, typhoid fever; and with a little more, typhus; and all in the same ward or hut. Would it not be far better, truer, and more practical if we looked upon disease in this light? for diseases, as all experience shows, are adjectives, not noun substantives.

But William Budd did not cause Miss Nightingale to alter her opinions. In an edition of *Notes on Nursing* published in 1909, when she was aged eighty-nine, the year before her death, the passage appears unchanged, except that it is now incorporated in the text.

The third edition of Murchison’s *Treatise*, which was published posthumously under the editorship of W. Cayley in 1884, still contains the word “pythogenic” and the idea it represents. Belief in spontaneous generation lingered on till after the end of the century. Perhaps its last flicker was in the article in which, in 1905, J. Butler Burke described the origin of what

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he thought to be living particles, in tubes of bouillon acted on by radium. He called them "radiobes," and regarded them as primitive forms of life.

The Swallowed Infection

Although William Budd emphasized the spread of typhoid by the excreta of those ill from the disease, his original view was that the ultimate spread of the infection was by the air; but the conception of spread by swallowing came before long. In 1858 M. W. Taylor of Penrith, an M.D. of Edinburgh, published a paper with the title "On the communication of the infection of Fever by Ingesta." He describes cases of a typhoid-like outbreak in Penrith and the surrounding countryside, which was spread by milk, and this seems to be the first description of what became one of the commonest modes of spread of the disease. Taylor concludes:

What I have more especially inferred is that the poisonous effluvia and cutaneous exhalations of fever may be absorbed by fluids, which, when used as ingesta, may constitute one means of spreading the disease. If this be a fact I conceive it to be a new one in the etiology of fever. . . .

G. Newman wrote in 1904 that up to that year more than one hundred and fifty epidemics had been traced to a polluted milk supply. In this paper he refers also to the third common method of typhoid infection, by the eating of shellfish, oysters, and others, which have been contaminated by sewage. A. Newsholme, who

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was at the time medical officer of health for Brighton, wrote in 1903:

In 1896 I summarized the evidence . . . and the inquiries . . . which led me to conclude that at least one-third of the cases of enteric fever originating in Brighton were caused by sewage-polluted molluscs.

He adds that in Brighton from 1894 to 1902, 241 cases were ascribed to this cause—about 26 per year. I myself, while working in hospital in Glasgow in 1911, looked after a number of patients who had been infected on a Glasgow Spring Holiday, at a place on the Ayrshire coast, by eating what in Scotland we call “wilks.”

Prevalence and Mortality

With the increase in knowledge the diagnosis of typhoid was now more reliable, and it became possible to get an idea of the number of people who died from it, and so of its prevalence, for it was not made noticeable till 1889. One of the early observations was that whereas typhus affected particularly the poor and wretched, typhoid attacked all classes alike. Prince Albert, the Prince Consort, died of it in 1861 at the age of forty-two, and the Prince of Wales, afterwards Edward VII, had a very severe attack in 1871, when he was thirty. In the decade 1871-80 the annual number of deaths in England and Wales per million living was 332. The number of cases would be about six times that figure, in all about 54,000 per year for Britain, which, in the middle of that decade, had a population

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of 27 millions. A city of the present size of Edinburgh would then have about a thousand cases annually. The yearly number of deaths fell progressively to 35 per million in the decade 1911-20. The late Professor A. W. Harrington once told me that when he was a resident assistant physician in Ruchill Fever Hospital, Glasgow, about the year 1905, eight wards were allotted to typhoid and two to diphtheria. When I came to work in the same hospital in 1910 these figures were reversed. By 1941-50 the deaths were down to 1.4 per million. According to the Registrar-General's figures the number of notified cases in 1911 was 13,800, and in 1947, 687, 412 of these being paratyphoid. Before present-day treatment the case-mortality was commonly between 12 per cent. and 20 per cent., and varied little with time or place. It has often been said that typhoid is comparatively mild in children; but this was not Hensch's experience, for he had an 11 per cent. mortality in 266 cases.

Here is a sidelight on the former importance of typhoid. Fifty years ago the medical textbook used by nearly all Scottish students was Osler's *Medicine*, a book which is as good to read as ever. In the sixth edition (1905), out of eleven hundred pages, fifty were given to typhoid; yet typhus had only four. A contributory cause, no doubt, was Osler's great interest in the disease. He makes special reference to its occurrence in war:

Typhoid fever has been one of the great scourges of armies. . . . In the Spanish-American War (1898)

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the report of the Commissioners shows that one-fifth of the soldiers in the national encampments had typhoid fever. In 90 per cent. of the volunteer regiments the disease broke out within eight weeks of going into camp. In the South African War (1899-1902) the British Army in South Africa lost 7991 men from typhoid fever; 7582 died of wounds. As in America, the disease was one of standing camps.

J. W. Fortescue, the historian of the British Army, said in his Cambridge lectures in 1914:

No man perhaps ever merited the epithet of "organizer of victory" better than Moses, if only through his standing order (which you will find in the book of Deuteronomy, xxiii, 12-14) that when an army was in the field, there should be appointed places for latrines outside the camp, and that all foul matters should be instantly buried. . . . To this day it may be said that the sanitary regulations of Moses have never been superseded.

The Bacillus and its Reactions

A new era arrived when C. J. Eberth in 1880 saw typhoid bacilli for the first time, in sections of lymphatic glands and spleen. In twenty-three post-mortem examinations after typhoid, he found them in the spleen twelve times, and in the mesenteric glands six times. In 1881 he examined seventeen more cases, and again found bacilli, while in twenty-six cases of other diseases there were none. Gaffky, in 1884, using Koch's cultural

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methods, grew the bacillus in pure culture twenty-five times. At first the only bacteriological method of investigation was by the isolation of the bacillus, and this was done with no great difficulty from different parts of the body, or body substances. In 1894 Pfeiffer had shown the destructive effect of antiserum on cholera bacilli injected into the peritoneal cavity of guinea-pigs. In 1896 H. E. Durham, at the instigation of Max Gruber, with whom he was working in Vienna, applied the method *in vitro*, using a prepared antiserum, for the recognition of typhoid bacilli. The most pronounced effect was the aggregation of the bacteria into clumps and the loss of motility. Typhoid bacilli from various sources were tested, and all reacted, but there was no reaction with any of the specimens of *B. coli*. Durham suggested that the test might be used in the reverse way, with an unknown serum and a known bacillus, and this was carried out by A. S. Grünbaum, also working with Gruber. Widal's similar investigation was done about the same time, and his is the name commonly associated with the test. The use of the agglutination test spread quickly, and it has remained of the greatest service. It came to be realized that a simultaneously negative agglutination reaction and negative blood culture would exclude a diagnosis of typhoid at any stage, with considerable certainty.

Carriers

One of the results of bacteriological investigation was the proof that a few people, who had had an

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attack of typhoid and had recovered completely, might nevertheless remain dangerous sources of infection. H. Kayser wrote a paper on this in 1906, and cited the case of a woman of forty, the owner of a bakery in Strassburg, who had had typhoid ten years earlier. Two of her employees developed the disease, and she was found to be a faecal carrier. In the second case the carrier was a rag-dealer who had had typhoid thirty years before. In all, he mentions six cases of carriers, all women, and some of them, including the baker, showing symptoms of gall-stones. In a postscript to this article Kayser mentions the case of a woman who, in a period of mental depression, committed suicide six months after recovery from typhoid. The gall-bladder contained enormous numbers of typhoid bacilli, but there were no gall-stones. The Ledinghams in 1908 recorded investigations in an asylum in which typhoid fever kept recurring. They found three faecal carriers. In the same year G. Dean described the case of a doctor who, twenty-nine years after an attack, had typhoid bacilli as the predominant organism in the stools. Also in 1908, the *British Medical Journal* referred to the investigations in a recent outbreak in the west end of Glasgow. This was found to have been disseminated by milk, infected by a healthy carrier of sixteen years' standing. One of the best-known of carriers was Mary Mallon, who was confined to hospital in New York for over twenty years, until her death (J. D. Rolleston). She appears in the literature as "Typhoid Mary."

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The source of infection in the faecal carriers is the gall-bladder, which is infected very early in the course of typhoid. How long the bacilli live there has not been established, but in some cases it may be for many years. Whether this happens in every case it is not possible to say, but I cannot recollect ever having seen the record of a sterile gall-bladder in a person who previously had had the disease. It would seem that in most instances the bacilli die in their passage down the intestine; but not so in the carriers. Continued excretion of bacilli in the urine is possible. In 25 per cent. of all cases of typhoid, shortly before or shortly after the temperature becomes normal, bacilluria without pus appears, but it is symptomless and transient, lasting only a few hours or a few days. The mechanism of this has not been satisfactorily explained. But urinary carriers are few. Harvey says that among 2808 men who had had enteric fever, and who were concentrated after the First World War in an Enteric Depot, 85 were found to be carriers—72 faecal and 2 urinary.

Reference might be made in passing to laboratory infections with the typhoid bacillus. Bulloch cites from Hirschbruch and Forthman (1919) the case of a laboratory assistant who sucked up a culture from a pipette. Symptoms developed $13\frac{1}{4}$ days later. They collected 57 similar cases. The typhoid bacillus is not a dangerous organism to work with, if proper precautions are taken, and the main risk is in the use of a pipette without an intervening rubber tube.

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Immunization

One of the right sections of the history of typhoid is the story of the development of active immunization, and with this the name of Almroth Wright is specially associated. He published his first article on the subject in 1896, in the same volume of the *Lancet* as contains Grünbaum's paper on agglutination; and he said that in this work he followed the methods introduced by Haffkine in the prophylaxis of cholera. He inoculated two officers of the Indian Medical Service. One of them was given three injections of killed bacilli, with an interval of two weeks and then of four weeks; and six weeks after the third dose living typhoid bacilli were injected. No disease developed. From the first, the figures showed that the case-mortality was reduced, but in prevention the results were not so good as those obtained in later years. In 1902 Wright reviewed the results of immunization in a number of Army units in various places, including some figures from the South African War. "In every case," he said, "there was at least a twofold reduction in cases of typhoid fever in the inoculated. In certain cases there was a reduction varying from a sixfold to a twenty-eight-fold reduction." There was also a striking diminution in case-mortality.

Sir William Leishman in 1912, in a lecture on anti-typhoid inoculation, which I heard, paid tribute to Wright's work, and said that it was because of his enthusiastic efforts that anti-typhoid inoculation played the important part it did. Leishman said also:

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The temperature used to kill the bacilli is of primary importance. In older days we killed them at 60° or 63° C. Further investigation showed that a vaccine killed at that temperature soon became inert, and lost its immunizing properties. This fact probably explained many defective results in South Africa. Now we kill at the lowest possible temperature which will kill in one hour, at 53° C.

In a recent book L. F. Hirst points out that the vaccine must be made from a properly chosen organism:

The failure to choose a suitable culture of the typhoid bacillus for immunizing an army might lead to the loss of a campaign. . . . In fact, the use of an inefficient vaccine made from a "rough" strain of *B. typhosus*, or one lacking in the V antigen, probably contributed to the defeat of the Italians in the Second World War.

Harvey gives some Army figures to show the effect of immunization. In the South African War, among inoculated men, there were 1758 cases, with 142 deaths (8 per cent.); among the uninoculated, 10,980 cases, with 1800 deaths (16.6 per cent.). Several years later there were convincing figures from the Army in India. Whereas before inoculation the annual admission rate for all India was 8.9 per 1000, with 1.58 deaths, this in 1913 had fallen to 2.3 admissions per 1000, and 0.25 deaths. In two military stations the admissions between 1909 and 1913 fell, in one from 11.5 to 0.6, and in the other from 26.0 to 1.7 per 1000.

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When the First World War broke out the Army was well inoculated against typhoid, and this defence proved highly effective. Enteric fever was quite a minor problem, except on Gallipoli; and there it was nearly all paratyphoid, against which there had been no immunization. Harvey gives the following table which compares the figures of the South African War and of the First German War:

	<i>South Africa</i> (1899-1902)	<i>First German</i> (1914-18)
Strength	208,226	2,000,000
Cases	57,684	20,139
Deaths	8,022	1,191
Case mortality (per cent.) .	13.9	5.9
Cases per 1000 (annual) .	105	2.35
Deaths per 1000 (annual) .	14.6	0.139

The reduction in the case-mortality, which was noticed from the early days of inoculation, continued. In the $4\frac{1}{4}$ years of war the British figures were, among the inoculated 4.5 per cent., and among the non-inoculated 18.3 per cent.; which showed that there had been no falling off in the virulence of the organism. The French and the Germans had a similar experience.

Paratyphoid Infections

I wish now to say something about paratyphoid infections. These produce a disease which is in every way similar to typhoid; less severe on the whole, but

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not necessarily mild, and sometimes fatal. The bacilli are easily differentiated from typhoid bacilli in the laboratory, but it would be difficult to distinguish the fevers on clinical grounds. Paratyphoid fever was first described by Achard and Bensaude in 1896. Their paper begins with the words:

We propose to show in this communication that there are infectious illnesses of which the clinical picture resembles that of typhoid fever, and in which the pathogenic agents present a close affinity to the bacillus of Eberth, but are sharply distinguished from it by certain characteristics.

They describe two cases, and reproduce the temperature charts, which show in each a characteristic fall by lysis. The first patient was a woman of twenty-four, who had a complicating infection of the urinary tract. The urine contained albumin and pus, and paratyphoid bacilli were grown from it. The second patient was an infant of seven months, who, in the course of a typhoid-like illness, developed an abscess in the right sterno-clavicular joint, from the pus of which paratyphoid bacilli were grown. Such paratyphoid cases were evidently not numerous, and are described in the medical journals of the next few years rather as rarities, the bacilli sometimes being called paracolon bacilli, as in Gwyn's early case. In the first half-dozen years after the original paper, there does not seem to be any record of a case in Britain. In 1904, however, R. T. Hewlett reckoned that about a hundred cases had been described

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in all. In 1900 and 1901 Schottmüller isolated two types, which came to be known as A and B. In its cultural reactions A is closer than B to the typhoid bacillus. Experience showed that the cases which occurred in Western Europe were usually of the B type, whereas the A bacillus was mainly known as a cause of enteric fever in the British Army in India. Paratyphoid was uncommon in Britain, and I can say from my own experience that, between 1910 and 1912, one of the Glasgow hospitals, admitting patients with enteric fever from half the city, did not have a case.

The Gallipoli Campaign (1915)

The British Army had an intensive experience of paratyphoid fever on the Gallipoli peninsula in 1915. Landings had been made in the spring of that year, and the occupation continued till the end of December. The sanitary conditions were bad, and dysentery and fever of the enteric type were extremely common. As experience in France showed, the Army was well immunized against T, but A and B were not added to the stock vaccine till early in 1916, after Gallipoli had been evacuated. In the chapter on the Enteric Fevers in the official *History of the Great War*, the writer says:

It is especially unfortunate that the severe conditions ruling throughout the Gallipoli operations made it impossible for those concerned to render or obtain as accurate information regarding the incidence of enteric as could have been desired, and definite fig-

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ures as to the relative proportions of T, A, and B, their respective incidence among the inoculated and the non-inoculated, and on other points, are lacking.

However, a good deal of this information could have been obtained from the records of the base hospitals. A few bacteriologists were sent to Malta in the autumn of 1915. I was one of these, and was posted to what was then the permanent military hospital of the island (Cottonera), to reopen the laboratory, which had been closed for some months. I still possess notebooks of the time, and can throw some light on the question of diagnosis. I previously summarized this information in a short article in 1938.

The Malta hospitals received patients from Gallipoli, and dysentery and enteric fever abounded, among the wounded in surgical wards as well as on the medical side. It was sometimes found that pyrexia, which apparently was caused by septic wounds, was in fact due to paratyphoid. Indeed, it would have been difficult to be sure that a soldier who had had any sort of illness had not really had an attack of paratyphoid fever. It was not universally recognized that paratyphoid was occurring, and some perplexing reports of agglutination tests done with the typhoid bacillus had been sent to the wards. When the tests were carried out against paratyphoid A and B the difficulties were at once resolved. It was desirable to make a diagnosis in as many cases as possible, so I concentrated on the agglutination tests, though making

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cultures when opportunity arose. After preliminary trials a dilution of 1-800 was used, with each of the three bacilli, T, A, and B. This was high enough to clear the agglutination level from T inoculation and to make positive results with A and B undoubted. The results were as follows, derived mainly from agglutinations, but with a few cultures included:

<i>Total men examined</i>	T+	A+	B+
619	9	98	104

This shows that of those cases of enteric fever 4 per cent. were typhoid, 46 per cent. paratyphoid A, and 50 per cent. paratyphoid B.

Three pages from these old laboratory notebooks have been reproduced, two showing agglutination tests and the third a post-mortem report. The first was an early set which was done with several dilutions of serum. The blood of eight patients were tested and seven gave a positive result, four for A and three for B. One of the patients died later and B bacilli were grown from the bile. This post-mortem examination showed what is not uncommon even in fatal cases of paratyphoid, changes in the Peyer's patches much less severe than in typhoid. The second plate shows the result of the examination of twenty bloods with a single dilution of 1-800. Seven gave agglutination of A and three of B; and one with a negative reaction agglutinated A a few days later. The third plate is of a post-mortem examination in a man who had had gunshot wounds, paratyphoid B fever, and dysentery. During life the serum

Aglyptinus (minorpi)

25/10/15

1 1/2 hours

Name	Date	B. typhonus				B. para. A				B. para. B				Remarks
		1:40	1:50	2:00	2:10	2:20	2:30	2:40	2:50	3:00	3:10	3:20	3:30	
1. Bell's	60	+	-	-	-	+	+	+	+	+	+	+	+	2 incubations (April 1915)
2. Rosall	8	(+)	-	-	-	+	+	+	+	+	+	+	+	2 incubations (Sept 1914)
3. Crowther	8	(+)	-	-	-	+	+	+	+	+	+	+	+	Entire in 1897: 2 incubations (July 1915)
4. Ellard	17	-	-	-	-	+	+	+	+	+	+	+	+	2 incubations (October 1914) (1 day overland)
5. Hillon	24	(+)	-	-	-	+	+	+	+	+	+	+	+	2 incubations (Nov 1914)
6. Savory	15	(+)	-	-	-	+	+	+	+	+	+	+	+	2 incubations (Feb 1915)
7. Wand	24	(+)	-	-	-	+	+	+	+	+	+	+	+	2 incubations (March 1915)
8. Whitlam	24	-	-	-	-	+	+	+	+	+	+	+	+	3 incubations (Dec 1914: Feb 1915)

* Wand died on 4/11/15: cysts of illu - specifically P. p.: no incubation - B. para typhonus B. para from file.

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Agglutination (microscopic)
Dilution 1-800. - 3 hours.

10/11/15

Ward	Name	Age	Height	Weight	Temp	Remarks
5	Allen	17	—	—	—	Nov 1914 (2)
5	Bryson	15	(+)	++++	—	Oct 1914 (2)
5	Carr	14	—	—	++++	Nov 1914 (2)
5	Davidson	15	—	—	—	April 1915 (2)
1	Duckworth	—	—	—	—	—
2	Elliott	15	—	—	—	—
5	Ferguson	15	—	++++	—	Dec 1914 (2)
5	Hunter	14	—	++++	—	Repeated & confirmed 16/4/15 Doubtful on 8/1/15
1	McIntosh	—	—	—	—	—
5	McIntosh	15	—	—	—	—
5	McIntosh	13	—	++++	—	April 1915 (2)
1	Murphy	—	—	—	—	—
5	Partridge	15	—	++++	—	April 1915 (2)
1	Potts	—	—	—	++++	—
5	Raphael	15	—	—	—	Died of dysentery 10/1/15 P.M. 16/1/15 8 years for 16/1/15
5	Santos	13	+++	—	++++	Dec 1914 (2)
4	Taylor	—	—	—	—	Not a clinical enteric
5	West	24	—	++++	—	June 1915 (3)
T	Gray	—	—	—	—	Reverted on 4/1/15
1	Pharaph	—	—	—	—	Reverted 28/3/16

January 1st 1916

Gunner B. 7.

S.S.W. Upper & lower limbs : paratyphoid B fever : dysentery

Wounds of R upper limb & L thigh.

Abdomen Congestion of ileum, more marked in cecum area of
2-3 inches in length : one large Peyer's patch markedly red.

No ulceration. Moderate congestion and considerable
thickening of whole of wall of great intestine, which is in a
dysenteric condition. No ulceration in large or small intestine.
Liver large, very pale, fatty : weighs 72 g. Spleen a little
enlarged : brownish & very soft.

Thorax Some hypostatic congestion of both lungs. Heart in
heart. Lungs normal.

Cultures - bile - B. paratyphoid B.
spleen - sterile

AD.

Par B grows from pieces in lgs. Hyphomycetes 2 B +

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showed B agglutination and the B bacillus was grown from the faeces. After death it was grown from the bile.

In a set of tests done on a day which is not shown the diagnosis with which the patient was admitted to hospital was noted in each case. There were eight paratyphoid cases out of the sixteen tested, and on admission they were diagnosed as, respectively, pyrexia (2), fever (2), pneumonia, influenza, dysentery (which the patient no doubt had), and debility. The medical officers would intend these to be no more than provisional diagnoses with which to send the patients on, but it shows how they could not be relied on for statistical information.

In 1919 L. Hirschfeld described a third variety of paratyphoid bacilli, which he called paratyphoid C. In his work as director of the General Laboratory of the Serbian Army he had first isolated this organism in 1916, and up to 1918 had found eighteen other cases. The clinical picture was of the usual enteric type, but the infection could be virulent, and the first patient died. In patients who had been inoculated with TAB vaccine, this bacillus was found more often than any other of the enteric group; but after C had been added to the vaccine, any positive cultures were obtained only from uninoculated persons.

Recent Enteric in Britain

There was speculation as to whether, after the infection of so many soldiers with the A bacillus, paratyphoid A fever would establish itself in Britain.

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It has remained of infrequent occurrence, but B is comparatively common, and indeed commoner than T. The Registrar-General's figures of enteric notifications for 1947, which I have already cited, show that in that year there were 275 cases of typhoid and 412 of paratyphoid. Dr. Matthew Fyfe, Medical Officer of Health for Fife, has kindly supplied me with figures of the number of cases of enteric fever which have occurred in the county of Fife since 1892. In the last twenty years, from 1934 to 1953, there were 55 cases of typhoid and 86 of paratyphoid (5 of A, and 81 of B). The proportions are much the same as in the general notifications for 1947. In contrast, in the first twenty years on the list, from 1892 to 1911, there were 1274 cases, presumably all typhoid.

Let me conclude with a College story. In the membership examination in January of this year (1954) there was a question in the general paper on the differential diagnosis of pyrexia. I think William Budd would have been pleased if he could have read the answer of one candidate who included typhoid among the fevers which do not now occur in Britain.

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REFERENCES

- ACHARD, C., and BENSAUDE, R. (1896), *Bull. et mém. soc. méd. d'hôp. de Paris*, 3^e sér. **13**, 820.
- BARLOW, H. C. (1839-40), *Lancet*, **1**, 838.
- BOTTOMLEY, G. (1853), *Lancet*, **1**, 535.
- BRETONNEAU, P. F. (1829), *Arch. gén. de méd.*, sér. **21**, 57-78.
- BUDD, W. (1856), *Lancet*, **2**, 617, 694; *Brit. med. J.* (1861), **2**, 457, 485, 523.
- BULLOCH, W. (1929), *System of Bacteriology* (M.R.C.), vol. IV, 42.
- BURKE, J. B., *Fortnightly Review*, Sept. 1905, 389.
- Chambers's Encyclopaedia* (1906), article "Hygiene," VI, 42.
- DEAN, G. (1908), *Brit. med. J.*, **1**, 562.
- DURHAM, H. E. (1896), abstr. in *Proc. Roy. Soc. Lond.*, **59**, 224.
- EBERTH, C. J. (1880), *Virchow Archiv. f. path. Anat. u. Phys. u. f. klin. Med.*, **81**, 58; (1881), **83**, 486.
- ELIOT, G. (1871-2), *Middlemarch*, ch. 76, ch. 18.
- FORTESCUE, J. W., *Military History*, p. 40: Cambridge, 1914.
- FYFE, G. M. (1954), personal communication.
- GAFFKY, G. (1884), *Mitth. a. d. kaiserl. Gesundheitsamte*, **2**, 372.
- GOODALL, A. L. (March-April 1954), *Bull. of the Hist. of Med.*, vol. XXVIII, 140.
- GRUBER, M. (1896), *Münch. med. Wehnschr*, p. 206.
- GRUBER, M., and DURHAM, H. E. (1896), *Münch. med. Wehnschr*, p. 285.
- GRÜNBAUM, A. S. (1896), *Lancet*, **2**, 806.
- GWYN, A. B. (1898), *Johns Hopkins Hosp. Bull.*, **9**, 54.
- HARVEY, D. (1929), *System of Bacteriology* (M.R.C.), vol. IV, 17-85.
- HENOCH, E., *Lectures on Children's Diseases* (trans. N.S.S. 1889), **2**, 322.
- HEWLETT, R. T. (1904), *Practitioner*, **72**, 173.

THE ENTERIC FEVERS

- HIRSCH, A. (1883), *Handbook of Geographical and Historical Pathology* (trans. N.S.S., 2nd ed., 1883), vol. 1, 618, 621.
- HIRSCHFELD, L. (1919), *Lancet*, **1**, 296.
- HIRST, L. F., *The Conquest of Plague*, p. 94: Oxford, 1950.
- History of the Great War: Medical Services, Pathology* (1923), p. 214.
- HUXHAM, J. (1739), *Essay on Fevers*, 2nd ed.: London, 1750.
- JENNER, W. (1849-51), *Medical Times*, vols. xx-xxiii (20 papers);
Lectures and Essays on Fevers and Diphtheria: London, 1893.
- KAYSER, H. (1906), *Arb. a. d. kaiserl. Gesundh.*, **24**, 176.
- Leading article, *Brit. med. J.*, 1908, **1**, 584.
- LEDINGHAM, A., and J. C. G. (1908), *Brit. med. J.*, **1**, 15.
- LEISHMAN, W. B. (1912), *Glas. med. J.*, **77**, 401.
- LOUIS, P. CH. A., *Recherches pathologiques et thérapeutiques sur la maladie . . . typhoïde*: Paris, 1829.
- MACLAGAN, T. J. (1867), *Edin. med. J.*, **13**, 297.
- MURCHISON, C. (1862), *A Treatise on the Continued Fevers of Great Britain*, 3rd ed.: London, 1884.
- NEWMAN, G. (1904), *Practitioner*, **72**, 55.
- NEWSHOLME, A. (1903), *Brit. med. J.*, **2**, 295.
- NIGHTINGALE, F. (1859), *Notes on Nursing*, p. 19.
- OSLER, W., *Principles and Practice of Medicine*, 6th ed., p. 57: London, 1905.
- PATRICK, A. (1914), *J. of Path. and Bact.*, **18**, 365; (1938), *J. of the R.A.M.C.*, **71**, 182.
- PERRY, R. (1836), *Edin. med. and surg. J.*, **45**, 64.
- PETIT, M. A., and SERRES, E. R. A., *Traité de la Fièvre entéromésentérique*: Paris, 1813.
- PFEIFFER, R. (1894), *Ztschr. f. Hyg. u. Infektionsk.*, **18**, 1.
- PFEIFFER, R., and ISSAEFF (1894), *Ztschr. f. Hyg. u. Infektionsk.*, **17**, 354.
- PROST, P. A., *Médecine éclairée par l'observation des corps*: Paris, 1804.

THE ENTERIC FEVERS

Review *Lancet*, 1853, **2**, 80.

ROLLESTON, J. D. (1938), *Brit. med. J.*, **1**, 1247.

SCHOTTMÜLLER, H. (1900), *Deutsch. med. Wchnschr.*, **26**, 511; (1901), *Ztschr. f. Hyg. u. Infektionsk.*, Bd. 36, 368.

SHERIFF, T. (1865), *Edin. med. J.*, **11**, 565.

SMITH, S. W., *The 1936 Outbreak of Typhoid Fever at Poole, Bournemouth and Christchurch*: Bournemouth, n.d.

STEWART, A. P. (1840), *Edin. med. and surg. J.*, **45**, 64.

TAYLOR, M. W. (1858), *Edin. med. J.*, **3**, ii, 993.

The Times, July 31, 1954: London.

WIDAL, F. (1896), *Bull. et mém. soc. méd. d'hôp. de Paris*, 3^e sér., **3**, 561.

WRIGHT, A. E. (1896), *Lancet*, **2**, 807; (1902), **2**, 651.

WRIGHT, A. E., and SEMPLE, D. (1897), *Brit. med. J.*, **1**, 256.

